Original Article

The role of salt taste receptors and its genomics in salt taste sensitivity and preference: A systematic review and meta-analysis.

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ARTICLE INFO

Article history:

Received 25 November 2022

Revised 29 November 2022

Accepted 30 November 2022

Keywords:

Hypertension

Salt taste receptor gene

Salt taste sensitivity threshold

Salt preference

Single nucleotide polymorphism

Abbreviations:

ENaC, Epithelial Sodium Channel (ENaC)

TRPV1, Transient Receptor Potential cation subfamily Vanilloid member 1 channel

SNPs, Single Nucleotide Polymorphisms

Rs, Reference SNP IDs

Highlights:

- Salt taste sensitivity threshold and preference is controlled by salt taste receptor channels.
- Any mutations in the salt taste receptor channels will result in impaired salt taste sensitivity threshold.
- Individual variation in salt perception and intake may be due to the SNP in salt taste receptor genes.
- A simple gustatory test of salt perception can help in the management of hypertension.

ABSTRACT:

Salt intake plays an important role in the development of hypertension. Regulation of salt intake is partially due to the genetic variation in salt taste receptor genes related to homeostatic sodium regulation and hedonic responses to salt taste. The main objective of our study is to evaluate the relationship between single nucleotide polymorphisms in salt taste receptor genes (ENaC & TRPV1) in salt taste sensitivity threshold and salt taste preference. A systematic search was performed covering PubMed database for English studies with humans using Mesh terms. The preparation of this paper was guided by the Preferred Reporting Items in Systematic Reviews and Meta-Analyses (PRISMA) reporting checklist. This systematic review was carried out following PRISMA guidelines and registered in PROSPERO. Three studies involving 427 participants were finally included in our study. The results revealed that single nucleotide polymorphisms in transient receptor potential cation channel subfamily V member 1 (TRPV1 gene) is significantly associated with salt taste sensitivity threshold and salt taste preference ($p<0.05$). SNPs in Epithelial sodium channel (ENaC gene) modified supra-threshold salt taste sensitivity. However, there is no significant association between SNPs in ENaC and salt taste sensitivity threshold. In conclusion based on the available studies on genomics of salt taste sensitivity and preference, further research on the role of SNPs in salt preference and intake may help in better understanding on the risk of hypertension.

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Cite as: Vishnu Shivam, Vengojayaprassad S and Shanmugavadivu R. The role of salt taste receptors and its genomics in salt taste sensitivity and preference: A systematic review and meta-analysis. The Journal of Medicine and Science 2022; 01(03): 17-22.

1. INTRODUCTION

Salt intake plays an important role in the development and management of hypertension [1]. Regulation of salt intake is partially due to the genetic variation in salt taste receptor genes related to homeostatic sodium regulation and hedonic responses to salt taste [2]. 2 Lingual cation channels have been identified as potential salt taste receptors: (i) Sodium-specific and amiloride sensitive Epithelial Sodium Channel (ENaC) and (ii) Transient Receptor Potential cation subfamily Vanilloid member 1 (TRPV1) channel [3]. Any genetic variation or single nucleotide polymorphisms of these genes will lead to higher salt taste threshold and lower salt sensitivity, thereby results in higher salt preference and intake. This explains the individual variation in salt taste perception and intake. As current knowledge about the risk factors of hypertension does not include the effect of polymorphisms in salt preference and intake, this review will help in understanding the potential role of these single nucleotide polymorphisms as a biomarker and in the development of targeted dietary therapy in the management of hypertension [4-7]. The main objective of our study is to identify the relationship between single nucleotide polymorphism of salt taste receptor genes (ENaC & TRPV1) in salt taste threshold and preference.

2. MATERIALS AND METHODS

2.1 Search strategy:

The current review is registered on the PROSPERO International Prospective register of Systematic reviews (CRD42022362804) and was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines. A literature search to identify articles evaluating the association of genetic variants in salt taste receptors with salt taste sensitivity threshold and preference was completed using a pre-determined search strategy in the PubMed and Researchgate databases. The exact search terms used were: ‘salt taste receptors’ AND ‘salt sensitivity’ AND ‘salt sensitivity threshold’ AND ‘taste receptor gene’ AND ‘salt taste receptor gene’ AND ‘blood pressure’ AND ‘hypertension’. The title and abstract of search results were screened for relevant articles, which were selected for full text evaluation by two authors independently (first and second author) using predetermined eligibility criteria.

2.2 Inclusion and Exclusion criteria:

Articles which assess the direct relationship between panels of SNPs in salt taste receptor genes ad psychophysical measure for salt taste modality were included. Articles which are not in English language, not relevant to our study, other than human studies, case reports, erratum, commentary and editorials were excluded.

2.3 Study selection and data extraction:

Following the removal of duplicates, studies were screened independently by two reviewers (first and second author) with discrepancies concluded by consensus agreement. The following data were extracted from eligible articles: (1) Study details (first author, publication date, country of origin); (2) Population characteristics (gender, age and ethnicity); (3) Single Nucleotide Polymorphisms

reported. The Newcastle-Ottawa scale (NOS) was used to assess the study quality and potential bias based on three domains. The NOS included 3 categorical criteria with a maximum score of 9 points. The quality of each study was rate using the following algorithms: ≥7 points were considered as "good", 2 to 6 points were considered as "fair" and ≤1 point was considered as "poor" quality. Quality assessment was checked independently by first two authors and any disagreements were solved by the third author.

2.4 Meta-Analysis:

Data-analysis was performed by first author and reviewed by third author. Data were extracted, where possible, in the form of genotype frequency distributions between single nucleotide polymorphisms genotyped in salt taste receptor gene and association with salt taste sensitivity threshold and preference.

A meta-analysis was performed to calculate overall risk of SNP in salt taste receptor gene with salt taste sensitivity threshold and preference. The number of SNPs genotyped and its association with salt taste sensitivity threshold and preference was entered into a dichotomous Mantel-Hanszel meta-analysis as shown in Figure 1 using RevMan 5.4 software (Cochrane Collaboration, Oxford, United Kingdom) to generate pooled risk ratio with 95% confidence intervals (CI). Genetic models were analysed using random effects model and quantified with the i^2 statistic.

3. RESULT

3.1 Study selection:

Figure 1 shows the PRISMA Flow diagram summarizing the results of the study selection process. Once duplicates were removed, reviews, case studies and others were excluded as mentioned before and shown in Figure 1. Full text studies investigating SNP panel and psychosocial measures of taste modality were reviewed by first two authors and only 3 articles were included in the final meta-analysis.

3.2 Study characteristics:

The characteristics of each included study are summarized in Table 1. A total of 42 SNPs from the two salt taste receptor genes were analysed in the included studies. The total sample size of the included studies was 427 participants of various ethnicities, aged 4-80 years of age were included. Among the included studies two studies had NOS quality assessment score of 8 and 1 has total NOS score of 9 as shown in Table 2 and they were considered as good quality. A summary of the assessment, including domain level judgments are presented in Table 2.

3.3 Meta-analysis:

43 SNPS from the two salt taste receptor genes (TRPV1 & ENaC) were genotyped in the included studies. 7 SNPs were replicated in the 3 studies which constituted the quantitative meta-analysis. The summary statistics for the association of SNPs and salt taste sensitivity threshold were presented in Figure 2. Table 2 includes pooled analysis for all participants of included studies. A non-significant low heterogeneity was observed in the meta-analysis outcomes with i2 = 37% (p = 0.20).

Statistically significant overall effect was found from the meta-analysis of SNP ($p<0.05$). The overall risk ratio is 0.28 (95% CI: 0.12 – 0.67, p = 0.004) which shows that 28% of individuals having the SNPs have impaired salt sensitivity threshold and preference.

4. DISCUSSION

These studies revealed that single nucleotide polymorphisms in salt taste receptor gene TRPV1 is significantly associated with salt taste threshold and preference (Risk Ratio: 0.28, 95% CI: 0.12-0.67, p = 0.004). The TRPV1 SNPs (rs4790522, rs222745, rs150908, rs161386, rs150908, rs4790151, rs877610) increases the risk of higher salt taste threshold and lower salt sensitivity by 28%, thereby leads to 28% risk of higher preference for salt. SNP in Epithelial sodium channel (ENaC gene) modifies supra-threshold salt taste sensitivity. However, there is no significant association between SNPs in ENaC and salt taste threshold.

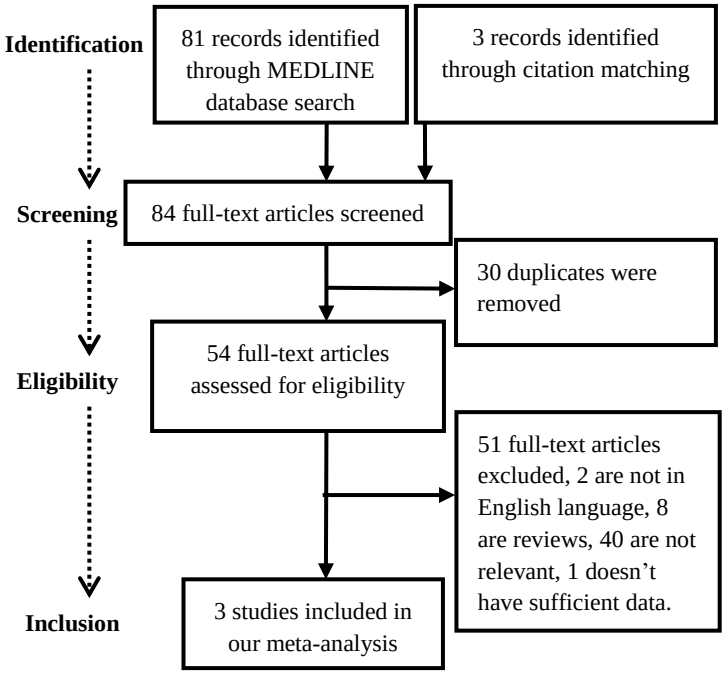

Figure 1 shows the PRISMA Flow diagram summarizing the selection process.

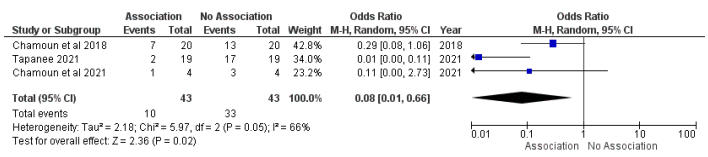

Figure 2 shows Forest plot of comparison: Association of salt taste receptor gene SNPs and Salt taste outcome

In conclusion, this study provides a new insight on the role of polymorphisms of salt taste receptor genes and their effects on salt taste threshold. Further, a simple gustatory clinical test of salt sensitivity threshold and perception can be used to assess the taste preference for targeted dietary management in hypertensive individuals. This study does have some limitations that the overall number of studies available for this review was limited. Despite the limitations, this represents a first systematic effort into the role of single nucleotide polymorphisms influencing salt threshold and preference.

Acknowledgements

We acknowledge the support provided by Department of General Medicine, Coimbatore Medical College and Hospital and ACP-India Chapter for their advice and feedbacks which proved invaluable in guiding the direction of the research.

Funding Source

None

Credit Authorship Contribution Statement

Vishnu Shivam: Conceptualization, Methodology, Screening, Writing, Formal Analysis, Visualization.
Vengojayaprassad S: Screening, Writing and Reviewing.
Shanmugavadivu R: Writing – Review and Editing.

Declaration of Competing Interest

The authors declare that there is no potential conflict of interest related to this article.

Peer-Review

The manuscript has been reviewed by

1. Dr. Charles Bronson, Associate Professor, Stanley Medical College, Chennai.
2. Dr. Raja M, Consultant Physician and Diabetologist, CM Speciality Hospital, Namakkal.

Supplementary material

Not applicable

REFERENCES:

1. Chamoun E, Liu AS, Duizer LM, Qi W, Feng Z, Darlington G et al. Single nucleotide polymorphisms in sweet, fat, umami, salt, bitter and sour taste receptor genes are associated with gustatory function and taste preferences in young adults. Nutr Res. 2021;85:40-46. doi:10.1016/j.nutres.2020.12.007

2. Chamoun E, Carroll NA, Duizer LM, Qi W, Feng Z, Darlington G et al. The Guelph Family Health Study. The Relationship between Single Nucleotide Polymorphisms in Taste Receptor Genes, Taste Function and Dietary Intake in Preschool-Aged Children and Adults in the Guelph Family Health Study. Nutrients. 2018; 10(8):990. doi:10.3390/nu10080990

3. Tapanee P, Tidwell DK, Schilling MW, Peterson DG, Tolar-Peterson T. Genetic Variation in Taste Receptor Genes (SCNN1B, TRPV1) and Its Correlation with the Perception of Saltiness in Normotensive and Hypertensive Adults. Int J Hypertens. 2021;2021:5559831. Published 2021 Jun 4. doi:10.1155/2021/5559831

4. Azinge EC, Sofola OA, Silva BO. Relationship between salt intake, salt-taste threshold and blood pressure in Nigerians. West Afr J Med. 2011;30(5):373-376.

5. Kirsten VR, Wagner MB. Salt taste sensitivity thresholds in adolescents: are there any relationships with body composition and blood pressure levels?. Appetite. 2014;81:89-92. doi:10.1016/j.appet.2014.06.001

6. Martinelli J, Conde SR, Araújo AR, Marcadenti A. Association between salt taste sensitivity threshold and blood pressure in healthy individuals: a cross-sectional study. Sao Paulo Med J. 2020;138(1):4-10. doi:10.1590/1516-3180.2019.0166.R1.02102019

7. Michikawa T, Nishiwaki Y, Okamura T, Asakura K, Nakano M, Takebayashi T. The taste of salt measured by a simple test and blood pressure in Japanese women and men. Hypertens Res. 2009;32(5):399-403. doi:10.1038/hr.2009.31

No.	Author, Year.	Region	Study design	Study Population	SNPs in Salt taste receptor gene	
					Total SNPs genotyped	SNPs associated with taste modality
1	Chamoun et al, 2018	Canada	Cohort study	125	20	6 (TRPV1 SNPs rs4790522, rs222745, rs150908, rs161386, rs4790151, rs877610)
2	Tapaneeet al, 2021	USA	Cross-sectional case control study	253	4	1 (TRPV1 SNP rs4790522)
3	Chamoun et al, 2021	Canada	Cohort study	49	19	2 (TRPV1 SNPs rs4790522, rs222745)

Table 1. shows characteristic features of included studies

No.	Author, Year.	NOS Quality assessment*			
		Selection	Comparability	Outcome/ Exposure	Total score
1	Chamoun et al, 2018	4	2	2	8
2	Tapanee et al, 2021	4	2	3	9
3	Chamoun et al, 2021	4	2	2	8

Table 2. shows the Quality assessment of studies included in the review

*Newcastle-Ottawa Scale – Total Scores: Low quality: 0–3; Medium quality: 4–6; and High quality: 7–9.

Graphical Abstract: